

CLAIMS

What is claimed is:

- 5 1. A pharmaceutical preparation for sustained-release of an active pharmaceutical ingredient after parenteral administration comprising:
 a multiplicity of coated microparticles, said coated microparticles comprising
 (a) core particles comprising said active pharmaceutical ingredient;
10 and
 (b) a first polymeric coating on said core particles formed from a first polymer-forming solution;
 wherein said active pharmaceutical ingredient forms a saturated solution within said coated microparticles after said administration; and
15 wherein said first polymeric coating is permeable to said active pharmaceutical ingredient during a sustained-release period from administration of said microparticles until the concentration of said active pharmaceutical ingredient contained within said microparticles is unsaturated.
- 20 2. The pharmaceutical preparation of claim 1, wherein diffusion of said active pharmaceutical ingredient across said first polymeric coating exhibits pseudo-zero-order kinetics during said sustained-release period.
- 25 3. The pharmaceutical preparation of claim 1, wherein said first polymeric coating is substantially degraded after said sustained-release period.
4. The pharmaceutical preparation of claim 1, wherein said first polymeric coating maintains structural integrity during said sustained-release period.
- 30 5. The pharmaceutical preparation of claim 1, wherein said microparticles are administrable via parenteral injection.

6. The pharmaceutical preparation of claim 5, wherein said microparticles have a maximum dimension between 20 µm and 800 µm.
7. The pharmaceutical preparation of claim 5, wherein said microparticles have a
5 maximum dimension between 40 µm and 400 µm.
8. The pharmaceutical preparation of claim 5, wherein said microparticles have a maximum dimension between 100 µm and 250 µm.
- 10 9. The pharmaceutical preparation of claim 1, wherein said active pharmaceutical ingredient is substantially insoluble in said first polymer-forming solution.
10. The pharmaceutical preparation of claim 1, wherein said active pharmaceutical ingredient is hydrophobic and said first polymer-forming solution is hydrophilic.
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11. The pharmaceutical preparation of claim 1, wherein said active pharmaceutical ingredient is hydrophilic and said first polymer-forming solution is hydrophobic.
12. The pharmaceutical preparation of claim 1, further comprising:
20 (c) a second polymeric coating on said first polymeric coating,
wherein said second polymeric coating is formed from a second
polymer-forming solution;
wherein said second polymeric coating is permeable to said active
pharmaceutical ingredient during said sustained-release period.
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13. The pharmaceutical preparation of claim 1, further comprising:
(c) a porous second polymeric coating on said first polymeric coating,
wherein said second polymeric coating is formed from a second
polymer-forming solution;
30 wherein said second polymeric coating defines pore regions which permit fluid
communication between a pore portion of said first polymeric coating and an external

environment, thereby allowing diffusion of said active pharmaceutical ingredient across said first polymeric coating in said pore regions; and

wherein said second polymeric coating defines non-pore regions which prevent fluid communication between a non-pore portion of said first polymeric coating and
5 an external environment, thereby inhibiting diffusion of said active pharmaceutical ingredient across said first polymeric coating in said non-pore regions.

14. The pharmaceutical preparation of claim 13, wherein said second polymeric coating is substantially impermeable to said active pharmaceutical ingredient in said
10 non-pore regions.

15. The pharmaceutical preparation of claim 13, wherein said second polymer-forming solution comprises pore-forming agents which dissolve to produce said pore regions after formation of said second polymeric coating.

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16. The pharmaceutical preparation of claim 1, wherein said first polymeric coating comprises a polymer or co-polymer including at least one monomer selected from the group consisting of sugar phosphates, alkylcellulose, hydroxyalkylcelluloses, lactic acid, glycolic acid, β -propiolactone, β -butyrolactone, γ -butyrolactone,
20 pivalolactone, α -hydroxy butyric acid, α -hydroxyethyl butyric acid, α -hydroxy isovaleric acid, α -hydroxy- β -methyl valeric acid, α -hydroxy caproic acid, α -hydroxy isocaproic acid, α -hydroxy heptanic acid, α -hydroxy octanic acid, α -hydroxy decanoic acid, α -hydroxy myristic acid, α -hydroxy stearic acid, α -hydroxy lignoceric acid, β -phenol lactic acid and polyvinyl alcohol.

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17. The pharmaceutical preparation of claim 12 or 13, wherein said second polymeric coating comprises a polymer or co-polymer including at least one monomer selected from the group consisting of sugar phosphates, alkylcellulose, hydroxyalkylcelluloses, lactic acid, glycolic acid, β -propiolactone, β -butyrolactone, γ -butyrolactone, pivalolactone, α -hydroxy butyric acid, α -hydroxyethyl butyric acid, α -hydroxy isovaleric acid, α -hydroxy- β -methyl valeric acid, α -hydroxy caproic acid, α -hydroxy isocaproic acid, α -hydroxy heptanic acid, α -hydroxy octanic acid, α -hydroxy

decanoic acid, α -hydroxy myristic acid, α -hydroxy stearic acid, α -hydroxy lignoceric acid, β -phenol lactic acid and polyvinyl alcohol.

18. The pharmaceutical preparation of claim 1, wherein said first polymeric coating is applied to said core particles by an air suspension technique.
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19. The pharmaceutical preparation of claim 1, wherein said first polymeric coating is applied to said core particles by a dip coating technique.
- 10 20. The pharmaceutical preparation of claim 1, wherein the weight of said first polymeric coating is between 0.1% and 200% of the weight of said core particle.
- 15 21. The pharmaceutical preparation of claim 1, wherein the weight of said first polymeric coating is between 2% and 60% of the weight of said core particle.
22. The pharmaceutical preparation of claim 1, wherein the volume of said first polymeric coating is between 0.1% and 200% of the volume of said core particle.
- 20 23. The pharmaceutical preparation of claim 1, wherein the volume of said first polymeric coating is between 2% and 60% of the volume of said core particle.
24. A method of sustained-release administration of an active pharmaceutical ingredient comprising administering parenterally a pharmaceutical preparation of any one of claims 1-23.
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25. The method of claim 24, wherein said pharmaceutical preparation is in the form of a suspension of said coated microparticles in a pharmaceutically acceptable carrier.
- 30 26. The method of claim 24, wherein said parenteral administration is selected from the group consisting of subcutaneous, intravenous, intramuscular and intraocular injection.

27. A method for producing a pharmaceutical preparation for sustained-release of an active pharmaceutical ingredient after parenteral administration comprising:

- 5 (a) forming core particles comprising said active pharmaceutical ingredient; and
 (b) forming a first polymeric coating on said core particles from a first polymer-forming solution;

wherein said active pharmaceutical ingredient forms a saturated solution within said coated microparticles after said administration; and

10 wherein said first polymeric coating is permeable to said active pharmaceutical ingredient during a sustained-release period from administration of said microparticles until the concentration of said active pharmaceutical ingredient contained within said microparticles is unsaturated.

15 28. The method of claim 27, wherein diffusion of said active pharmaceutical ingredient across said first polymeric coating exhibits pseudo-zero-order kinetics during said sustained-release period.

20 29. The method of claim 27, wherein said first polymeric coating is substantially degraded after said sustained-release period.

30. The method of claim 27, wherein said first polymeric coating maintains structural integrity during said sustained-release period.

25 31. The method of claim 27, wherein said microparticles have a maximum dimension between 20 μm and 800 μm .

32. The method of claim 27, wherein said microparticles have a maximum dimension between 40 μm and 400 μm .

30 33. The method of claim 27, wherein said microparticles have a maximum dimension between 100 μm and 250 μm .

34. The method of claim 27, wherein said active pharmaceutical ingredient is substantially insoluble in said first polymer-forming solution.

5 35. The method of claim 27, wherein said active pharmaceutical ingredient is hydrophobic and said first polymer-forming solution is hydrophilic.

36. The method of claim 27, wherein said active pharmaceutical ingredient is hydrophilic and said first polymer-forming solution is hydrophobic.

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37. The method of claim 27, further comprising:

(c) forming a second polymeric coating on said first polymeric coating from a second polymer-forming solution;

wherein said second polymeric coating is permeable to said active 15 pharmaceutical ingredient during said sustained-release period.

38. The method of claim 27, further comprising:

(c) forming a porous second polymeric coating on said first polymeric coating from a second polymer-forming solution;

20 wherein said second polymeric coating defines pore regions which permit fluid communication between a pore portion of said first polymeric coating and an external environment, thereby allowing diffusion of said active pharmaceutical ingredient across said first polymeric coating in said pore regions; and

25 wherein said second polymeric coating defines non-pore regions which prevent fluid communication between a non-pore portion of said first polymeric coating and an external environment, thereby inhibiting diffusion of said active pharmaceutical ingredient across said first polymeric coating in said non-pore regions.

39. The method of claim 38, wherein said second polymeric coating is 30 substantially impermeable to said active pharmaceutical ingredient in said non-pore regions.

40. The method of claim 38, wherein said second polymer-forming solution comprises pore-forming agents which dissolve to produce said pore regions after formation of said second polymeric coating.
- 5 41. The method of claim 27, wherein said first polymeric coating comprises a polymer or co-polymer including at least one monomer selected from the group consisting of sugar phosphates, alkylcellulose, hydroxyalkylcelluloses, lactic acid, glycolic acid, β -propiolactone, β -butyrolactone, γ -butyrolactone, pivalolactone, α -hydroxy butyric acid, α -hydroxyethyl butyric acid, α -hydroxy isovaleric acid, α -hydroxy- β -methyl valeric acid, α -hydroxy caproic acid, α -hydroxy isocaproic acid, α -hydroxy heptanic acid, α -hydroxy octanic acid, α -hydroxy decanoic acid, α -hydroxy myristic acid, α -hydroxy stearic acid, α -hydroxy lignoceric acid, β -phenol lactic acid and polyvinyl alcohol.
- 10 42. The method of claim 37 or 38, wherein said second polymeric coating comprises a polymer or co-polymer including at least one monomer selected from the group consisting of sugar phosphates, alkylcellulose, hydroxyalkylcelluloses, lactic acid, glycolic acid, β -propiolactone, β -butyrolactone, γ -butyrolactone, pivalolactone, α -hydroxy butyric acid, α -hydroxyethyl butyric acid, α -hydroxy isovaleric acid, α -hydroxy- β -methyl valeric acid, α -hydroxy caproic acid, α -hydroxy isocaproic acid, α -hydroxy heptanic acid, α -hydroxy octanic acid, α -hydroxy decanoic acid, α -hydroxy myristic acid, α -hydroxy stearic acid, α -hydroxy lignoceric acid, β -phenol lactic acid and polyvinyl alcohol.
- 15 43. The method of claim 27, wherein said core particles are prepared by high pressure compaction.
- 20 44. The method of claim 27, wherein said core particles are prepared by macrocrystal formation.
- 25 45. The method of claim 27, wherein said first polymeric coating is applied to said core particles by an air suspension technique.
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46. The method of claim 27, wherein said first polymeric coating is applied to said core particles by a dip coating technique.
- 5 47. The method of claim 27, wherein the weight of said first polymeric coating is between 0.1% and 200% of the weight of said core particle.
48. The method of claim 27, wherein the weight of said first polymeric coating is between 2% and 60% of the weight of said core particle.
- 10 49. The method of claim 27, wherein the volume of said first polymeric coating is between 0.1% and 200% of the volume of said core particle.
- 15 50. The method of claim 27, wherein the volume of said first polymeric coating is between 2% and 60% of the volume of said core particle.